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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,370	02/21/2001	Etsuro Ogata	OGATA4	9907
1444 7590 07/27/2007 BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, NW SUITE 300 WASHINGTON, DC 20001-5303			EXAMINER HARRIS, ALANA M	
			ART UNIT 1643	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

09/763,370

Applicant(s)

OGATA ET AL.

Examiner

Alana M. Harris, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 2-6,8-15,25-30 and 32 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-6,8-15,25-30 and 32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application
- ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Response to Arguments and Amendments***

1. Claims 2-6, 8-15, 25-30 and 32 are pending.

Claims 8 and 32 have been amended.

Claims 2-6, 8-15, 25-30 and 32 are examined on the merits.

### ***Withdrawn Objection***

#### ***Claim Objections***

2. The objection of claim 8 because the term "osteoblastsor" on line 4 was misspelled has been withdrawn in view of Applicants' amendment to the said claim.

### ***Withdrawn Rejection***

#### ***Claim Rejections - 35 USC § 112***

3. The rejection of claims 8, 10 and 32 under 35 U.S.C. 112, second paragraph, designated as c., e. and g., respectively in the Action mailed November 1, 2006 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of the amendment submitted May 1, 2007.

***Maintained Grounds of Objection***

***Specification***

4. The objection of the amendment filed May 17, 2006 and May 1, 2007 under 35 U.S.C. 132(a) because it introduces new matter into the disclosure is maintained and made.

a. Applicants assert "[t]he narrative on page 8, ...line 6 describes testing the progress of patients with prostatic cancer without bone metastasis.", see Remarks submitted May 1, 2007, page 12, 3<sup>rd</sup> paragraph. Applicants conclude the amendment filed May 17 does not contain new matter. This argument has been carefully considered, but found unpersuasive.

Applicants have pointed out a limited example that does note "...prostatic cancer patients with bone metastasis and ...prostatic cancer patients without bone metastasis." However, this example reads on prostate cancer and cannot be extrapolated to provide support for the instant claims that broadly read on a method of diagnosing amelioration and/or exacerbation of metastasis of malignant tumor to bone in a patient with *cancer*, which includes any and every type of cancer. Moreover, the original specification cites on page 9, lines 5-8, "Z value is defined by (measured value - average for the patients with bone metastasis)/(standard deviation of a patient without bone metastasis)."

Applicants' noted in the Remarks filed May 17, 2006, bridging paragraph of pages 12 and 13 the English translation of the Japanese application revealed a translational error, however Applicants have not presented objective evidence supporting the alleged error. Moreover, the Examiner cannot read the Japanese

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language. Consequently, one of ordinary skill in the art cannot verify whether or not the Z value did in fact use an average **without** bone metastasis. Accordingly, the objection is maintained.

### ***Maintained Rejections***

#### ***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. The **NEW MATTER** rejection of claims 2-6, 8-15, 25-30 and 32 under 35

U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained and made.

a. Applicants argue traversal of the instant rejection based on the arguments presented in the section numbered 3 on the instant Action. Applicants further arguments asserting the Z value would not make sense as presented in the original specification, see page 9, lines 5-8, "as one would not compare patients with bone metastasis to patients without bone metastasis.", see page 13 of the Remarks. These arguments and points of view have been carefully considered, but found unpersuasive. As noted in the response earlier Applicants point out an example, which reads on prostate cancer and cannot be extrapolated to provide support for the instant claims that broadly read on a method of diagnosing amelioration and/or exacerbation of metastasis of malignant tumor to bone in a patient with *cancer*, which includes any and every type

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of cancer. Moreover, the original specification cites on page 9, lines 5-8, "Z value is defined by (measured value - average for the patients with bone metastasis)/(standard Applicants have not presented objective evidence supporting the alleged error and the Examiner cannot read the Japanese language. Consequently, one of ordinary skill in the art cannot verify whether or not the Z value did in fact use an average **without** bone metastasis. Accordingly, the rejection is maintained.

b. Applicants have claim 8 to include the recitation "wherein a layer crossover index indicates amelioration of the patient's condition". Applicants assert support for this amendment can be found on page 9, lines 20-38 of the specification, see page 14 of the Remarks, 1<sup>st</sup> full paragraph. Foremost the text on page 14 ends at line 28 and not 38 as indicated by Applicants and there is no mention of "layer". The Examiner assumes Applicants intended to use the word, lower. Notwithstanding, a review of the particular section of the specification does not note a lower crossover index. However, on page 10 of the specification Applicants cite "[t]he crossover index was 0.596 in the CR [complete remission] group but 0.002 in the PD [progression of disease] group", see lines 21-24. It seems as if a lower crossover index is indicative of the disease was found to have progressed and according to the specification, see page 9, lines 18 and 19; page 10, lines 21-24. This is in contrast to what Applicants suggest and there is no support for Applicants' conclusion statement newly added to claim 8, a [lower] crossover index indicates improvement in the patient's condition. There is not corresponding information provided to support the amendment to the claim. Applicants should delete the new matter.

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c. Applicants have claim 8 to include the recitation "...using at least one of a formative marker that reflects the activity of osteoblasts or at least one of a marker that reflects the activity of osteoclasts,". Applicants have not indicated where support for this amendment can be found in the specification. The claim now contemplates the implementation of more than one osteoblast marker and more than one osteoclast marker for the evaluation of the efficacy of drugs for cancer disease treatment. A review of Example 1 beginning on page 8 notes the BALP marker (bone formation marker and osteoblastic marker) and osteocalcin marker. Example 2 serum BALP and serum osteocalcin markers were measured, see page 11 and Example 3 shows the use of BALP, ICTP (marker of bone resorption and osteoclasts) markers with serum CA 15-3 measured, see page 15 of the specification. There is not corresponding information provided to support the amendment to the claim. Applicants should delete the new matter or pointedly express by page and line number where support for this method is listed.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. The rejection of claims 2-6, 8-15, 25-30 and 32 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained and made.

a. Claims 6, 8 and 30 are vague and indefinite in the recitation "and determining a crossover index by dividing said Z value for osteocalcin by said Z value for ..., said crossover index and said ICTP level providing a diagnosis...".

Applicants assert the use of the crossover index is explained in detail on page 8, line 6 of the specification and claim 8 has been amended to recite a lower crossover index is indicative of amelioration of the patient's condition, see page 14 of the Remarks, 1<sup>st</sup> full paragraph. These points of view have been carefully considered, but found unpersuasive.

The information listed on page 8, line 6 of the specification does not absolve the instant rejection. The amendment to claim 8 does not resolve the indefiniteness of claims 6, 30, the instant claim and those that depend from them. The newly amended language of claim 8 is not supported by the specification as alleged by Applicants and what is listed in the specification, particularly page 10, lines 21-24 is contravene to the claim language of claim 8. Accordingly, the rejection is maintained for the reasons of record and listed herein.

b. Claims 2-6, 8-17 and 25-30 continue to be vague and indefinite because it is not clear from the claims how the two markers are used in ascertaining efficacy of a drug and the method steps are not clear.

Applicants have amended claim 8 in order to obviate the instant rejection. This has been carefully considered, but found unpersuasive.

The Examiner has carefully reviewed the specification, particularly page 8, line 6 of the specification and notes it does not absolve the instant rejection. The amendment

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to claim 8 does not resolve the indefiniteness of claims 6, 30, the instant claim and those that depend from them. The newly amended language of claim 8 is not supported by the specification as alleged by Applicants and what is listed in the specification, particularly page 10, lines 21-24 is contravene to the claim language of claim 8. Accordingly, the rejection is maintained for the reasons of record and listed herein.

d. Claim 32 continues to be vague and indefinite because the method steps read on measuring a marker for bone formation and a marker for bone resorption, ICTP, see lines 6-9. However, the conclusion step only cites ICTP values as the determinant useful for assessing progression of cancer metastasis.

Applicants simply respond to the instant rejection citing the marker for bone resorption comprises ICTP and the specific marker for bone formation is not cited meaning any bone formation marker can be used in the method. This response has been carefully considered, but is persuasive.

Listing of bone formation markers would not clarify the issue at hand, which is it not clear if the bone formation marker listed in lines 6 and 7 of the claim is of consequence in the method determining progression of disease when it seems the said progression is based solely on ICTP. Moreover, it is not clear what variants are being analyzed and what are ICTP values. Applicants are requested to clarify.

e. Claim 32 continues to be vague and indefinite in the recitation "the improvement" in line 6 of the claim.

Applicants assert claim 32 has been amended to correct for the lack of antecedent bases, indefinite language and is a Jepson-type claim and based on the

manner at which the claim is written, infer the rejection should be withdrawn. These points of view have been carefully considered, but found unpersuasive.

It is still not clear what one of ordinary skill in the art is supposed to assess as improved, the recitation lacks antecedent bases or what value is indicative of improvement. Furthermore, the claim does not address how the improvement comprising observing ICTP values over an undefined time demonstrating the progression of disease satisfies the evaluation of the efficacy a cancer drug, inhibition of metastasis and amelioration of metastasis. Applicants' claim continues not to be clear and definite.

### ***Conclusion***

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm, with alternate Fridays off.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

**ALANA M. HARRIS, PH.D.**  
**PRIMARY EXAMINER**



Alana M. Harris, Ph.D.  
18 July 2007